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Palliative Sedation in End-of-Life Care

Metropolia University of Applied Sciences
Bachelor of Healthcare in Nursing
Degree Programme in Nursing
Bachelor's Thesis
20 November 2023

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Title	Palliative Sedation in End-of-Life Care
Number of Pages	32 pages + 2 appendices
Date	20 November 2023
Degree	Bachelor of Healthcare
Degree Programme	Degree Programme in Nursing and Health Care
Instructor	Anna-Kaisa Partanen

Adequate symptom relief ought to be the standard of care for terminally ill. In spite of excellent palliative care, some patients experienced intolerable, uncontrollable pain and suffering from refractory symptoms. Palliative sedation was considered an acceptable treatment at the end of life for refractory symptoms.

The purpose of this study was to described the used of palliative sedation in end-of-life care as well as the drugs used in palliative sedation. This study aimed to provide further information and gain more knowledge on the utilization of palliative sedation in end-of-life care that will guide nurses and other health care practitioners in their scope of practice.

The articles were synthesized from the credible databases CINAHL and PubMed. Total of 15 academic articles including five qualitative and ten quantitative studies were reviewed. The articles included were published between Jan 2013 – Sep 2023. This study utilized descriptive literature review as a researched method and the data were analyzed using inductive content analysis.

The result of the study showed that the main indication of palliative sedation was to treat refractory symptoms. The sedative drugs utilized in palliative sedation were benzodiazepines particularly midazolam and anti psychotic neuroleptic such as haloperidol. In addition, non sedative drugs were also used in palliative sedation such as opioids.

This study will introduce palliative sedation as treatment of refractory symptoms. It will increase the knowledge of nurses on refractory symptoms and further understand the drugs utilize in palliative sedation to treat patients with terminal illness. The approach to patient treatment is multidisciplinary, thus it is in the best interest to be equipped with the necessary scientific knowledge and skills to carry out their task.

The Turnitin program was utilized to checked the origin of this study, which produced a similarity percentage within acceptable limits.

Keywords	end of life care, palliative care, palliative sedation, terminal illness, refractory symptoms

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1 Introduction

The key component of end-of-life care is the provision of effective pain management. It is especially difficult to achieve adequate symptom relief in terminally ill patients who have tried every other form of therapy without success. The administration of sedative drugs may be considered when traditional symptom control is insufficient (Ziegler et al. 2018: 2.) Murillo-Zamora et al (2020) presents Enck statement that the term palliative sedation was first utilized to relate the practise of symptom control through the administration of sedative medications in the early 1990s. Palliative sedation focuses on decreasing a patient's level of consciousness in order to treat persistent symptom (Murillo-Zamora, Garcia-Lopez, Santiago-Ruiz, Chavez-Lira and Guzman-Esquivel 2020: 2.)

The incidence of palliative sedation use is increasing recently as it is now considered to be essential to provide relief from suffering prior to death. The National Hospice and Palliative Care Organisation believes that palliative sedation is a choice that patients, family members, and medical professionals should think about to relieve intractable and intolerable suffering in patients who are close to death (Diez-Manglano et al. 2020: 305-306.) Patients who are close to death frequently display a wide range of symptoms, such as delirium, anxiety, pain, agitation, terminal restlessness, dyspnea, and emotional and physical suffering. Sedation therapy is a viable option to ease suffering if symptoms become intolerable and refractory despite comprehensive and multidisciplinary palliative care (Caraceni et al. 2018: 34.)

For all patients, but especially for those with terminal conditions, adequate symptom alleviation is a key component of medical care. Symptoms that are either physical or psychological may continue to be unmanageable in certain patients despite thorough management of such issues. Sedation near the end of life is legitimate and frequently employed therapeutic strategy minimizing the severity of the suffering and persistent symptoms (Schur et al. 2016: 1.) Despite recent developments in palliative medicine, sedation is still seen as a necessary treatment for managing persistent symptoms such as severe agitated delirium or dyspnea and relieving unbearable distress in terminally ill patients (Leboul et al. 2017: 2). Situations involving the dying are very sensitive. Evaluation of symptoms and decision-making are extremely difficult during a painful period, therefore, all the experts involved must work together to gather the data required

to examine refractoriness (Calvo-Espinos, De Gaona, Gonzalez, De Galarreta and Lopez 2015: 622.)

Patients experience in the end of life is influenced by a variety of elements, including the actions and treatment decisions made by the professionals caring for the patient. In the end of life, one must take into account a decision-making process that prioritises patient comfort, manages the effectiveness of therapies, and provides care in accordance with the standard from a palliative perspective (Campos-Calderon et al. 2016: 1.)

The purpose of this study is to describe the use of palliative sedation in end-of-life care as well as the drugs use in palliative sedation. Therefore, the aim of the study is to provide further information and gain more knowledge in the utilization of palliative sedation in end-of-life care that will guide nurses and other health care practitioners in their scope of practice.

2 Palliative sedation for terminally ill

Palliative care is a key element of integrated, patient-centered health services. It is a universal moral obligation to alleviate severe health-related suffering, whether it be psychological or physical. Palliative care must therefore be accessible at all levels of care and may be required for a variety of reasons, including end-stage chronic illnesses, cancer, heart disease, severe organ failure, and extreme frailty associated with advanced age (WHO: 2020.) This method reduces patients suffering while also supporting medical staff who must deal with the difficulties of treating refractory symptoms in the latter stages of a patient's terminal illness (Tan, Li, Wu & Zhang 2022: 2.) According to Beller et al. (2018), in the final hours or days of life of a terminally ill, sedation is intended to relieve refractory symptoms that cannot be managed with other means. Healthcare professionals must have a strong foundation in therapeutic communication skills and relevant information to support the palliative care principles (Beller, Van Driel, McGregor, Truong and Mitchell 2018: 3.)

The key terms utilized in this study are palliative care, palliative sedation, end-of-life care, terminal illness & refractory symptoms.

2.1 Terminal Illness

Terminally ill patients may develop different symptoms throughout the final hours and days of life. When the illness reaches the terminal phase, it is incurable and progressive as well as demise is imminent. These symptoms could turn resistant that may not be able to control by palliative and other supportive therapies intended specifically for such symptoms (Beller et al. 2018: 3.) Stefania M. Maci defines terminal illness as persistent or ailment that is fatal to a patient and for whom there is no treatment (Maci 2021: 220). A patient who is terminally ill is not receiving treatment to prolong their life. This includes the final 12 months of life, which are commonly referred to as the end-of-life period (Hanna et al. 2022: 1484.) It is an untreatable illness for which there is no adequate treatment and which is probably expected to result in imminent death (Subih et al. 2022: 2).

2.2 Palliative care and end-of-life care

Palliative Care is a multidisciplinary, integral and specialized medical care. The primary objective is to reduce symptoms and enhance patient’s quality of life when dealing with life-threatening, terminal and progressive diseases. All those who can benefit from it should be given access to palliative care as soon as possible, considering its positive impacts on everyone's comfort, alleviation of suffering and quality of life. Controlling symptoms and maintaining quality of life is crucial and extremely important during the final 3-6 months of terminal illness (Peralta, Castel-Branco, Reis-Pina, Figueiredo, and Dourado 2022: 1-2.)

World health organization described palliative care as a method to enhance the quality of life for patients and their families who are coping with issues associated with terminal illness. It prevents and lessen suffering by early detection, precise evaluation and management whether the symptoms are psychological, physical and existential suffering. In order to alleviate suffering, problems other than physical symptoms must be addressed. It offers a network of support to enable the patient to lead an active life until death. Numerous illnesses necessitate palliative care. Most patients in need of palliative care have chronic respiratory conditions, cardiovascular diseases, or cancer. Pain and breathing issues are two of the most prevalent and serious symptoms that people experience requiring palliative care. Opioids are necessary for the treatment of pain. Breathlessness is among the numerous common and distressing physical symptoms

that opioids can help with. Early symptom management is morally required to reduce suffering and uphold a person's dignity (WHO 2020.)

End-of-life care, as a component of palliative care, aims to maintain the quality of life for patients and their families by providing comprehensive management of all symptoms, including psychological, physical and existential suffering. It focuses on the final hours or days of life and involves deliberations on medical procedures such as delaying or not receiving a particular cancer treatment, resuscitation methods, and symptom management as well as decisions regarding palliative sedation. In the end of life, clinical judgment and prior expertise constitute a major part in guiding decisions, there are certain clinical and technical criteria that can also be used (Luna-Meza et al. 2021:2.)

The provision of palliative care services to patients in need is rapidly increasing globally since terminal illness is a major threat. Palliative care is typically necessary for chronic illnesses like cancer, chronic respiratory disorders, and cardiovascular disease services (Subih et al 2022: 2.) Patients may experience changes in their level of consciousness, either as an effect of different pharmacological treatments or related to symptom or disease progression. Clinicians may purposefully lower some patients level of consciousness by giving them sedatives and/or analgesics, particularly if their symptoms tend to worsen toward the end of their lives. As a result of one or more symptoms that are resistant to therapy, this technique attempts to reduce patients intractable suffering (Krooupa et al. 2020: 84.)

2.3 Sedation in palliative care

In the last hours or days of a patient life, some terminally ill patient may develop intolerable suffering that is refractory to palliative therapy. It may be difficult to manage symptoms and experience a peaceful death. Palliative sedation is considered a valuable therapeutic option for terminally ill patients whose refractory symptoms cannot be relieved despite aggressive measures. As described by the European Association for Palliative Care, sedative medication is used to alleviate existential suffering In the final stages of life (Mercadante, Porzio, Valle, Aielli and Casuccio 2013: 861.) The goal of sedation in palliative care is to induce unconsciousness and state of reduced or absent awareness, minimizing intractible suffering that would otherwise be unmanageable (Schildmann, Meesters & Bausewein 2022: 373).

Palliative sedation is well recognised and ethical medical procedure utilizing sedative drugs to purposely reduce consciousness of the patient to treat refractory and manage intolerable symptoms. It is clearly different practice from physician-assisted suicide and euthanasia, which are distinguished by similar concepts, intents, methods, and results. The prevalence of palliative sedation differs globally mostly due to variations in clinical practice patterns and care environments. This vast range may also be influenced by mixed cases in comparable settings, the degree to which palliative sedation standards are followed, and the level of skill of medical practitioners (Prado et al. 2018: 2.) This palliative care approach has been in use for many years, the fluctuating occurence varies from 2 to 52 percent, that could be determined by different factors like environment, population, religion, cultural as well as institutional policies. This approach is not based on timely and appropriate decision-making, but on the actual needs of patients (Mercadante et al. 2013: 861.)

Palliative sedation is either intermittent or continuous sedation as to its type. Continuous palliative sedation involves purposely inducing patient’s unconsciousness until death but different from euthanasia. According to a study, patients' survival times are not shortened by continuous palliative sedation, and it is not risky enough to carefully adhere to the principle of double effect. The increasing trends of continuous deep sedation are consistent with earlier advancements of other end of life opinions, like increased symptom relief by using life-prolonging medications, despite doctors judgments that this is an atypical clinical practice (Ziegler,Schmid, Bopp, Booshard and Puhan 2018: 1052.) Intermittent palliative sedation, otherwise known as respite or temporary sedation, is a variation on continuous palliative sedation whereby patient is awakened after a certain time during which the medication is withdrawn. According to a study, intermittent palliative sedation permits awareness reversibility and can be administered safely for several months (Won et al. 2019: 66.) Ocassionally, patients have been given this medication to help them relax with the goal of removing the sedation after a set amount of time (Rodrigues-Miranda et al. 2015: 277). Early in the course of the patient's therapy, transient or respite sedation may be necessary to offer momentary relaxation until the anticipated benefits of other therapeutic techniques are obtained (Garetto, Cancelli, Rossi & Maltoni 2018: 952). The resources provided by the clinical context and the practitioners' experience with palliative care are related to the variations in sedation practices (Ziegler et al. 2018: 6).

The decision making process in sedating a patient was frequently made in accordance with a plan or an evaluation of the patient's condition by a multidisciplinary team that

was knowledgeable about the patient's condition or by experts qualified to take part in such decisions (Abarshi et al. 2017: 225.) Sedation therapy is given consistently for at least an hour or intermittently for more than twenty-four hours in the final two weeks of patient’s life even if it was not administered at the time of death (Schur et al. 2016: 2). There are numerous drugs that can be used to induce palliative sedation, and there are different protocols or guidelines that can be followed when doing so. The patient's symptom presentation and the doctor's preference determine the drug to be taken. Benzodiazepines and neuroleptics are sedatives that can be used to treat delirium but not to relieve pain. Opioids are frequently used for analgesia or the treatment of dyspnea. Decisions on the type of sedation and dosage are made in consultation with the patient or their families, and they must to be documented. Many drugs are frequently used for prolonged sedation, usually in the context of critical care. Benzodiazepines particularly midazolam and neuroleptics are some of these drugs. But opioids are well-established for managing terminal patients' dyspnea as well as for controlling pain, and medical professionals may use them in addition to sedatives (Willard & Wiencek 2022: 51.) Different medication classes are acknowledged to be suitable for palliative sedation. The most frequent and often drugs prescribed for palliative sedation are benzodiazepines, specifically midazolam (Prado et al. 2018: 2.) Regardless of prior usage of sedative or neuroleptic medications, midazolam is administered intravenously or subcutaneously with a dose of 20-30 milligrams per day. The dosages of medications are titrated to achieve a safe and sufficient reduction in consciousness to alleviate suffering. Consequently, regular, meticulous monitoring of treatment and results is necessary (Gamblin et al. 2020: 34.)

In line with the protocol for sedative usage described by the European Association for Palliative Care's (EAPC), patients level of consciousness should be assessed as included in the routine evaluations both before and after the administration of sedative medication. By doing this, the effects of over- or under-sedation are avoided, and proportionality criteria are met. Observer-rated measures are often used to track states of consciousness in situations when sedatives and analgesics are routinely administered. In these study, the majority of the instruments consist of a single item with a categorical grading that represents level of consciousness reduction. Patients response to increasing intensity stimulation are usually used to assess these levels. This type of scale structure has benefits in terms of simplicity and usability, making it possible to quickly carry out repeated administrations, therefore closely monitor reactions to the use of sedatives and analgesics. However, it may result in overlaps

that might not always indicate mutual exclusivity across several states of consciousness. In addition, the development of protocols and recommendations for sedation is aided by the use of reliable and legitimate observational measures for determining consciousness. Subsequently, enhances communication between healthcare providers, and makes it easier to compare study data and findings (Krooupa et al. 2020: 84 - 85.)

Furthermore, the Richmond Agitation and Sedation Scale (RASS) often use to determine the depth of sedation in hospital setting which is the clearest and least time-consuming and most user friendly scale (Garetto et al 2018: 952). The RASS (see fig 1) was formulated in a medical scale to assess agitation, alertness and sedation level. It is commonly utilized in preventing over- and undersedation for ventilated patients, therefore this can be used in hospital setting. This scale consists of 10 points with a range from negative 5 to 4 resulting to a comprehensive interpretation for each score. Zero score describes alert and calm patient, spontaneously paying attention to the caregiver. Positive points represent level of agitation, ranging from +1 to +4, representing restlessness, agitation, combativeness and pronounced agitation. Negative points represent sedation level, with −1 manifesting drowsiness, as evidenced by not being fully alert, maintained awakening described by greater than 10 s, with eye response to voice. Light, moderate, and deep sedation including unarousable are described in levels -2 to -5 (Boettger et al. 2019: 149.)

Table 2: Richmond Agitation-Sedation Scale[a]

Score	Term	Description	
+4	Combative	Combative or violent, with immediate danger to self or staff	Proceed to CPOT Assessment
+3	Very agitated	Pulls or removes tube(s) or catheters; aggressive	
+2	Agitated	Has frequent nonpurposeful movements, fights ventilator	
+1	Restless	Anxious and apprehensive but not aggressive	
0	Alert and calm	Alert and calm	
−1	Drowsy	Awakens to voice stimulation, with eye opening/contact >10 seconds	
−2	Lightly sedated	Briefly awakens to voice stimulation, with eye opening/contact <10 seconds	
−3	Moderately sedated	Has movement or eye opening to voice stimulation but no eye contact	
−4	Deeply sedated	No response to voice stimulation but has movement or eye opening to physical stimulation	Repeat RASS in 1 h
−5	Unarousable	No response to voice or physical stimulation	

Fig 1. (Richmond Agitation-Sedation Scale (RASS) adapted from Bardwell, Brimmer & Davis 2020: 18)

2.4 Refractory symptoms indicating the use of palliative sedation

As death approaches, terminally ill patients may experience severe psychological, physical, or existential suffering in the end of life. Sometimes symptoms might become refractory, meaning that all potential treatment options have been tried and failed, or the risk-benefit ratio has become unacceptable, or the patient has not received the findings in a timely manner. In such cases, palliative sedation may be an option (Belar et al. 2020: 296.) Refractory symptom is the main indication of palliative sedation (Garetto 2018: 953). Refractory pertains to the symptoms that persist even after aggressive palliative care measures in the context of end-of-life care (Gilbertson, Savulescu, Oakley & Wilkinson 2022: 2).

The most frequent refractory symptoms experienced by patient with terminal illness are dyspnea, delirium, pain and existential suffering or the most typical reason of palliative sedation is delirium. Existential suffering is a complex problem whose features are distinct from those of physical or psychological symptoms. It is not confined to the terminal phase and could follow a varying or complex problem and is difficult to manage even in a healthy individual. A multidisciplinary team of experts should carefully evaluate and reassess the choice to administer palliative sedation in response to existential suffering on a regular basis. This team should concentrate on addressing intractable symptoms, offering psychological support and spiritual guidance, and implement intermittent rather than continuous sedation (Maltoni, Scarpi & Nanni 2014: 390.)

3 Purpose, Aims and Research Questions

The purpose of this study is to describe the use of palliative sedation in end-of-life care as well as the drugs use in palliative sedation. Therefore, the aim of this study is to provide further information and gain more knowledge in the utilization of palliative sedation in end-of-life care that will guide nurses and other health care practitioners in their scope of practice.

For the purpose of directing descriptive review, the following research questions were developed:

1. What is the use of palliative sedation in end-of-life care?

2. What are the drugs use in palliative sedation?

4 Methodology and Methods

Research is a systematic and critical study. In conducting research, a researcher should adhere to scientific procedures with the goal of providing answers to questions about nursing phenomena (LoBiondo-Wood and Haber 2018: 6-9.) It is a type of systematic approach which employs organised techniques for responding to inquiries or resolving issues with the intention of creating, acquiring, and making use of information that will be helpful to many such as conducting nursing research, participating in specialised studies, and consistently creating evidence to support and help clients and nursing practise. As a result, it improves knowledge and aids nurses in comprehending, implementing, and following evidence-based practices (Polit and Beck 2022:2.) Research methodology is the methodical examination of the research procedure. It addresses the science and philosophy of research methods as well as general rules for conducting research (Thomas 2021:29.) This study applied qualitative methodology to produce a descriptive literature review that describes the use of palliative sedation in end-of-life care as treatment of refractory symptoms.

4.1 Data Collection Method

The authors conducted article screening in collecting data needed in this study. To gather primary studies and academic articles, the two academic databases were utilized CINAHL and Medline. This study used descriptive literature review and inductive content analysis was utilized to collect and analysed data from relevant articles. Academically reviewed articles for the use of palliative sedation and drugs use in palliative sedation were screened to select the articles that answers the research questions. The researchers utilized Boolean search phrases and used relevant search article key terms for each database. Furthermore, the researchers also seek the assistance and help of the university's informatician to searched for the articles to ensure reliability and accuracy. Inclusion and exclusion criteria were formulated to acquire the relevant articles needed for this study. Limiters were applied throughout the article search using English as the main language and the year of publication were limited from 2013 to 2023. Articles were excluded if they did not address the study's questions, were not academic article, or were older than 2013. All 15 articles pertinent to the study were read in full text and selected based on the set inclusion criteria. The PRISMA flow chart (figure 1) presents the search strategy clearly.

4.2 Data search and selection

In this study, the PICo framework was utilized to form search sentences for database search as shown on Table 1. PICo in qualitative study describes patient with terminal illness as the population in the study. Furthermore, the study's interest was the palliative sedation in end-of-life care therefore, the context was related to the used of palliative sedation and drugs used in palliative sedation. Using the key terms palliative care, sedation, end-of-life care, terminal care, terminal illness, and sedate, articles were collected from databases. During the searched, boolean operations such as "AND" and "OR" were applied. The following key phrase combinations were used: "palliative care AND sedation AND end of life care OR terminal care AND sedate* OR terminal illness." Limiters like English language, and year of publication from 2013 to 2023 were also used to further hone the searched results. In addition to the restrictions listed above, there were other inclusion and exclusion criteria used to choose the articles, such as: publications about palliative care, articles that answered the study question, academic and peer reviewed articles. The primary sources for the chosen literature were all academic articles.

PICo	Definition
Population	Patient with Terminal illness
Interest	Palliative sedation
Context	Use of palliative sedation in end-of-life care and the drugs use in palliative sedation

Table 1. PICo (population, interest and context) framework

The searched was performed in two academic databases: CINAHL and Medline. Data selection process was presented through Prisma diagram in Figure 2. By utilizing key terms and Boolean technique, initial searched yielded 131 articles. Limiters were applied to reduce the number of searched results using year of publication between 2013-2023 and published in English. After applying the limiters, the searched result yielded 120 articles then we had excluded 11 articles. Articles were then selected by title which further reduced the volume of articles into 73 and another 47 other articles were excluded. The title of the selected articles was relevant to the used of palliative sedation in end-of-life care. Further screening continued by the group members by reading the abstract of the articles. The process further reduced the articles into 57. The selection criteria for abstract were relevant to the formulated study questions. Finally, 41

selected articles were read in full text and evaluated based on its relevance to the study. After further evaluation, the number of articles was further reduced by excluding 26 articles that were not directly answering the study questions. We came up with 15 articles that were arranged in a table according to the year of publication and author, title of article, name of publisher, methodology and methods utilized for the study, participants included, main outcomes and limitations as seen in appendix 1. Among 15 articles, twelve were authored by physicians and terminally ill patients were the subject of the study conducted and nurses were included as participants, whereas three articles were nursing articles authored by registered nurses. The detailed results from the data base search were presented in table 2.

Furthermore, the researchers looked over these articles to improve the accuracy of data gathering. The Journal's value as a sourced were assessed via the publication forum (JuFo). The Finnish scientific community created the Publication Forum (JuFo), a classification of publication avenues that aids in the evaluation of the calibre of research. It is a website that rates the credibility of journals on a scale from 0 to 3, whereby, the higher the number means the journals are more credible. The 15 articles chosen for this study was of level 1 and 2 (Julkaisufoorumi 2023.)

Database	Search Items	Limiters	Total number of hits	Selected based on Title	Selected based on abstract	Selected based on whole text
CINAHL	Palliative care AND sedation AND end-of-life care OR terminal care AND sedate* OR terminal illness.	Published date 2013-2023 Published in English	76	41	33	25
MEDLINE	palliative care AND sedation AND end-of-life care OR terminal care AND sedate* OR terminal illness.	Published date 2013-2023 Published in English	55	32	24	16
Records in Total			Total n= 131	Total n= 73	Total n= 57	Total n= 41
Records removed based on inclusion and exclusion criteria						n=26
Total number of studies included						**N=15**

Table 2. Data base search results

The screening procedure was graphically outlined in the PRISMA flow diagram as shown below (see fig 2). By summarizing decisions made at different points during the descriptive literature review, before beginning the selection process, it counts the number of items found explicit. At each level, the number of articles was kept track of. The PRISMA chart also offers thorough details and a list of all referred publications that were acceptable for the literature review's final input.

PRISMA flowchart of included articles

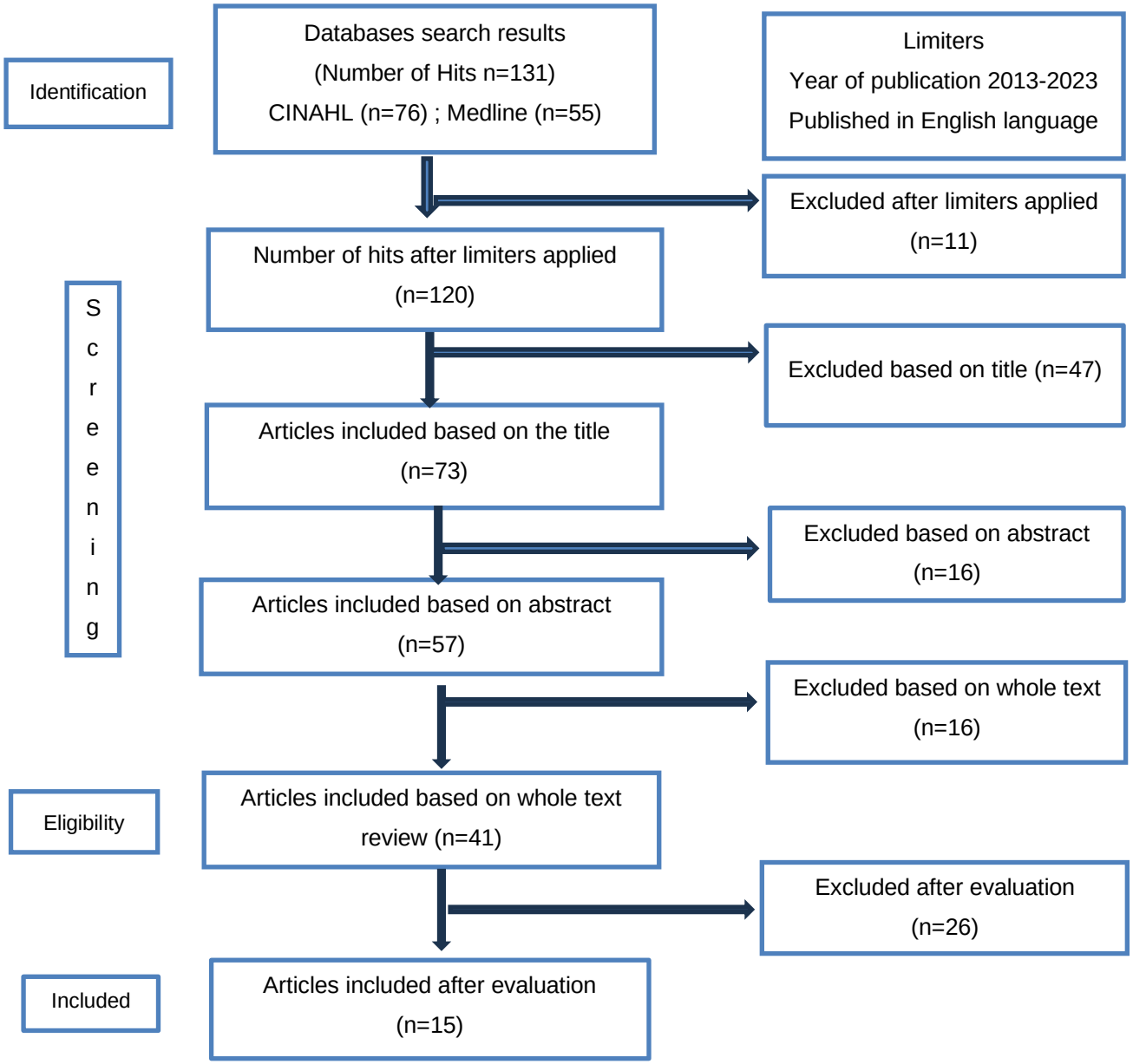

Fig. 2 Prisma flowchart on the process of data selection

The summary of criteria for inclusion and exclusion in this study was shown on Table 3. For a clear comprehension of which publications to choose or not, as well as the justifications for those criteria, the used of the inclusion and exclusion criteria was beneficial in this process. The inclusion criteria were studies published within 10 years between 2013 to 2023, peer-reviewed primary studies and written in English language. The exclusion criteria were studies published earlier than 2013, secondary studies, reviews, commentaries and written in other languages than English.

Inclusion	**Exclusion**
Published within 10 years (2013-2023)	Published articles more than 10 years old and articles earlier than 2013.
Academic articles and peer reviewed	Non-Academic articles, reviews and commentary
Published in English	Published in other language
Studies focusing on palliative sedation of terminally ill and end of life care	Studies not related to palliative sedation and end of life care such as euthanasia

Table 3. Inclusion and exclusion criteria

4.3 Data analysis

The analysis process reduced the volume of the text that was gathered and seeks understanding by identifying and grouping related categories. The authors stayed true to the text and each stage of data analysis was conducted repeatedly thus maintaining the reliability and quality of the analysis. The purpose of data analysis was to arrange the gathered information, derived meaning from it, and draw reasonable conclusions. The data were presented in words, enabling interpretation of the results (Bengtsson 2016: 9-11.)

This study utilized inductive content analysis, a qualitative methodology aiming to generate understanding of the significance of the data set content. It does not take into account content occurrences while determining statistical relationships between various content elements or calculating frequencies. It was a useful method to use since there was lacking existing research in this particular area of study (Vears & Gillam 2022: 112.)

The collected data from 15 articles were organized in a five-column table with titles assigned to each column. Meaning unit was the initial step in coding which was the extension of the cognitive process of comprehending. After closely analysing the text, the authors arranged the data into a broader sense (Vears & Gillam 2022: 117-118.) It was the smallest unit with some insights and the group of phrases or paragraphs addressed the research questions outlined in the aim of the study and the aspects were related to each other. It was given the first column which displayed the findings of the research done on the specific article and the original phrase was extracted without alteration. Two authors separately analysed the articles to derive a more in-depth analysis of the meaning units then the third author went over the articles again confirming analysis reliability and validity (Bengtsson 2016: 11-12.)

After the meaning units have been determined, the authors examined all aspects of the content ensuring that the text were in line with the aim of the study. The original text was read once more in conjunction with the meaning units final list. This indicate that the number of words were reduced while maintaining the unit content (Bengtsson 2016: 12.) The reduction/coding assigned for the study results of the associated article was listed in the second column. The third column contained the subcategory that was created using the code from the previous column. Generic categories were created on the fourth column that was obtained from the subcategory of the previous column. The main category, which consisted of the study questions, was given the fifth column. At this point, the information gathered was consistent with the research questions. The sample content analysis done for this study was shown on table 4.

Table 4. Sample content analysis table

Meaning units (original text)	Reduction/Coding	Sub Category	Generic Category:	Main Category
Of note was the fact that continuous deep sedation was associated with a significant survival risk in patients with agitated delirium. This is consistent with the previous finding that agitated delirium was an independent risk factor for serious complications of palliative sedation (Yokomichi et al. 2022:197.) "Is it now just to cushion the agitation or is it really now a full-blown psychosis where I really want to subdue the patient signifcantly. Or do I want to sedate him now, so, really just for the purpose of, I don't know, an MRI (Meesters et al. 2021:4). Regarding patient characteristics (Table 1), groups in both the PCU and ICU showed similar characteristics with a comparable mean age, the major reasons for palliative sedation in both settings were pain (Shen et al. 2018: 1533).	Consistent with the findings delirium is the most common symptom indicating the use of palliative sedation. Patient manifesting symptom of agitation where sedation is required by Physicians. Pain is another indication of Palliative sedation in different setting.	Symptom of delirium. Symptoms of agitation.	To relieve psychological refractory symptoms	Use of palliative sedation in end-of-life are
When things are getting really on top of you, an injection that will put you to sleep, might just help you get over that really bad period. And patients and doctors often refer to that as giving somebody Midazolam [a sedative] for time out (Anquinet et al. 2013: 542) Opioids were maintained, if previously given for other reasons (pain or dyspnea), via nonoral routes, with no intention to sedate. If the physician judged it appropriate, the second step was started, increasing the dose of midazolam up to 30-60 mg/day (Mercadante et al. 2013: 862.)	Benzodiazepines particularly midazolam are used as sedative for terminally ill patient who is in really bad period. Aside from midazolam, another palliative drug use is opioids to relieve mainly pain and dyspnea.	The most often used palliative drug was benzodiazepines particularly Midazolam. Opioids were also prescribed in the last week of life.	Sedative drugs Non sedative drugs	Drugs use in palliative sedation

During the data analysis, all selected 15 articles were read meticulously and the data were categorized in two main categories “use of palliative sedation in end-of-life care” and “drugs use in palliative sedation” which were in line with the research questions. The results from use of palliative sedation in end-of-life care were further divided into three generic categories to relieve psychological refractory symptoms, to relieve physical refractory symptoms and to relieve existential suffering using inductive content analysis. Relief of psychological refractory symptoms were found in 14 articles, whereas relief of physical refractory symptom were found in 13 articles. Lastly, 4 articles mentioned the relief of existential suffering. On the other hand, the second main category drugs use in palliative drugs yielded two generic categories sedative drugs which was found in 11 articles compared to 6 articles mentioned with the generic category non-sedative drugs. The main categories and generic categories were presented on table 5.

Main Category	Generic Category:
Use of palliative sedation in end-of-life care	To relieve psychological refractory symptoms To relieve physical refractory symptoms To relieve existential suffering
Drugs use in palliative sedation	Sedative drugs Non-sedative drugs

Table 5. Main categories and Generic categories

Afterwards, the researcher scrutinized the coded data thoroughly. The subcategories were further processed after all the text had been coded. Subcategories that were sufficiently distinct from one another stood alone, whereas similar categories were combined into one. To best account for the depth and complexity of the data, the subcategories were grouped and ungrouped. This was done without being repetitive or dissecting the data into so many tiny categories that the meaning is lost (Vears & Gillam 2022: 122.) The generic categories and subcategories created was shown on table 6.

Generic Category:	Sub-Category
To relieve psycho-logical refractory symptoms	Symptom of delirium. Another documented symptom is anxiety. Palliative sedation is also used for symptoms of agitation.
To relieve physical refractory symp-toms	Dyspnea is the second most common refractory symptom. Pain also indicates the use of palliative sedation. Other physical symptom is fatigue.
To relieve existen-tial suffering	Feeling of demoralization, despondency, sense of dependency and loss of will to live, hopelessness, being battle weary and mental exhaustion.
Sedative drugs	The most often used palliative drug was benzodiazepines par-ticularly Midazolam. Haloperidol is also frequently use in palliative sedation.
Non-sedative drugs	Opioids were also prescribed in the last week of life.

Table 6. Generic and sub-categories

After completing inductive content analysis, the relevant extracted units were systematically reviewed and the analysed data were ready for reporting with the inclusions of main categories, generic categories and subcategories as presented in table 7 Units of Analysis based on the selected articles. Overall, the authors extracted thirty five (n=35) original text from the selected articles, ten (10) subcategories, five (5) generic categories were generated from the subcategory and lastly, two (2) main categories.

Main Category:	**Use of palliative sedation in end-of-life care**			**Drugs use in palliative sedation**	
Generic Category:	**To relieve psychological refractory symptoms**	**To relieve physical refractory symptoms**	**To relieve existential suffering**	**Sedatives drugs**	**Non-Sedative drugs**
Sub- Categories:	Symptom of delirium. Another documented symptom is anxiety. Palliative sedation is also used for symptoms of agitation.	Dyspnea is the second most common refractory symptom. Pain also indicates the use of palliative sedation. Other physical symptom is fatigue.	Feeling of demoralization, despondency, sense of dependency and loss of will to live, hopelessness, being battle weary and mental exhaustion.	The most often used palliative drug was benzodiazepines particularly Midazolam. Haloperidol is also frequently use in palliative sedation.	Opioids were also prescribed in the last week of life.
Units of Analysis (Selected Articles)	**1,2, 3,4,5,6, 7,8,9,10,11,12,13,15**	**1,2,3,4,5,6,8,10,11,12,13,15**	**2,4,6,9,15**	**1,4,5,6,7,9,10,11,12,13,15**	**1, 4,5,7,8,13**

Table 7. Units of analysis based on the lists of selected articles

5 Results

5.1 Summary of Data

In this study, 15 research articles included were all academic articles and peer reviewed. The study was conducted between 2013 and 2022 and chosen from journals on palliative care, participants were terminally ill patient, families of terminally ill, healthcare professionals such as nurses and physicians who handled patients with terminal illness. The study group sizes varied from 13 to 4276 terminally ill patients cared for.

The descriptive literature review comprises research publications that were carried out in 13 different countries. Ten studies were from Europe: Austria (Schur, Weixler & Gabl 2016), Germany (Schildmann, Meesters & Bausewein 2022 & Meesters, Grune & Bausewein 2021), Belgium, Netherlands and United Kingdom (Anquinet, Van der Heide & Bruinsma 2013), Italy (Mercadante, Porzio & Valle 2013 & Caraceni, Speranza & Spoldi 2018), United Kingdom (Vivat, Qureshi & Harrington 2019), Netherlands (Van Deijck, Hasselaar & Verhagen 2016), France (Gamblin, Berry & Bruneel 2020), and Spain and Argentina (Diez- Manglano, Perez & Fenoll 2020).

Four from Asian countries: Korea (Eun, Hong, & Bruera 2017 & Won, Chun & Seo 2019), Taiwan (Shen, Chen & Cheung 2018) and Japan (Yokomichi, Yamaguchi & Maed 2022), Lastly, one article from South America, Brazil (Prado, Gomes & Uson 2018).

Ten quantitative studies (Diez- Manglano et al. 2020, Shen et al. 2018, Schur et al. 2016, Schildmann et al. 2022, Mercadante et al. 2013, Prado et al. 2018; Yokomichi et al. 2022, Caraceni et al. 2018, Van Deijck et al. 2016 & Gamblin et al. 2020) and five qualitative studies (Eun et al. 2017, Anquinet et al. 2013, Meesters et al. 2021, Vivat et al. 2019 & Won et al. 2019). The summary of the data findings is presented in table 8.

Journal/Source name	Methods	Year of Publication	Study Location
Journal of pain and symptom management (7 articles) BMC palliative care (4 articles) Palliative medicine (4 articles)	Qualitative (5 articles) Quantitative (10 articles)	2013 – 2 2016 – 2 2017 – 1 2018 – 3 2019 – 2 2020 – 2 2021 – 1 2022 – 2	Spain and Argentina (1) Austria (1) Germany (2) Italy (2) France (1) Belgium, Netherlands & UK (1) Netherlands (1) UK (1) Brazil (1) Korea (2) Taiwan (1) Japan (1)

Table 8. Data findings

5.2 Use of palliative sedation in end-of-life care

According to Shen et al. (2018), the indication of palliative sedation was to induced unconsciousness or reduced awareness without hastening death, thus relieving suffering (Shen et al. 2018. 1531). The selected articles described similar results as to use of palliative sedation in end-of-life care mainly to treat refractory symptoms whether to relieve physical, psychological symptoms and existential suffering. Using inductive content analysis, three generic categories were obtained to answer the research question “what is the use of palliative sedation in end-of-life care?

To relieve psychological refractory symptoms were identified from 14 articles (Diez-Manglano et al. 2020, Eun et al. 2017, Shen et al. 2018, Schur et al. 2016, Schildmann et al. 2022, Anquinet et al. 2013, Meesters et al. 2021, Mercadante et al. 2013; Vivat et al. 2019; Prado et al. 2018; Yokomichi et al. 2022; Won et al. 2019; Caraceni et al. 2018 & Gamblin et al. 2020). Whereas to relieve physical refractory symptoms were obtained from 13 articles (Diez- Manglano et al. 2020, Eun et al. 2017, Shen et al. 2018, Schur et al. 2016, Schildmann et al. 2022, Anquinet et al. 2013, Mercadante et al. 2013, Prado et al. 2018, Yokomichi et al. 2022, Won et al. 2019, Caraceni et al. 2018, Van Deijck et al. 2016 & Gamblin et al. 2020). Furthermore, there were five articles mentioned to relieve existential suffering (Eun et al. 2017, Schur et al. 2016, Anquinet et al. 2013, Vivat et al. 2019 & Gamblin et al. 2020) but only one (Anquinet et al. 2013) among the five articles had specified the symptoms of existential suffering.

5.2.1 Psychological refractory symptoms

Among psychological refractory symptoms included mainly delirium (Diez- Manglano et al. 2020; Shen et al. 2018; Schur et al. 2016; Mercadante et al. 2013; Prado et al. 2018; Yokomichi et al. 2022; Won et al. 2019 & Caraceni et al. 2018). Delirium was a symptom which palliative sedation most frequently needed. Prodromal indications were frequently misdiagnosed or poorly treated, therefore prompt assessment is crucial. (Garetto et al. 2018: 953). Agitation was also common symptom beneficial with the used of palliative sedation (Schildmann et al. 2022; Anquinet et al. 2013; Vivat et al. 2019 and Gamblin et al. 2020). Furthermore, three articles mentioned anxiety as indication of palliative sedation (Schildmann et al. 2022; Anquinet et al. 2013 and Meesters et al. 2021).

5.2.2 Physical refractory symptoms

Another generic category was physical refractory symptoms. The most frequently reported indication was dyspnea (Diez- Manglano et al. 2020; Eun et al. 2017; Schur et al. 2016; Anquinet et al. 2013; Mercadante et al. 2013; Prado et al. 2018; Yokomichi et al. 2022; Won et al. 2019; Caraceni et al. 2018; Gamblin et al. 2020). Dyspnea was a disorder that typically manifests in the final month of life and was often misdiagnosed and mistreated by medical professionals. Nonetheless, a number of research projects with this particular focus have been carried out (Garetto et al. 2018: 953.)

Another frequently documented indication of palliative sedation was to relieve symptom of pain (Diez- Manglano et al. 2020; Shen et al. 2018; Schur et al. 2016; Schildmann et al. 2022; Anquinet et al. 2013; Yokomichi et al. 2022; Won et al. 2019; Caraceni et al. 2018). While pain was not often regarded as the only refractory reason to use palliative sedation, it was commonly linked to agitation and dyspnea, therefore it needs to be appropriately assessed using appropriate verbal or non-verbal scales (Garetto et al. 2018: 953). Fewer studies resulted to the physical symptoms of fatigue (Anquinet et al. 2013 and Yokomichi et al. 2022).

5.2.3 Existential suffering

Another indication of palliative sedation was described by Schur et al. (2016) as existential suffering that has been specified by Anquinet et al. (2013) as symptoms of demoralization, despondency, sense of dependency, loss of will to live and

hopelessness. There was substantial discussion pertaining to the use of palliative sedation for existential suffering. Although palliative sedation was only thought to be clinically suitable for patients whose symptoms were unresponsive, it was important to keep in mind that this was unquestionably a very delicate topic worthy of great reflection. Because existential discomfort was associated with psychological, psychiatric, and psychopharmacological problems, its management was highly specialized and multidisciplinary, and it was likely less evolved than the treatment of physical symptoms (Garetto et al. 2018: 953.)

5.3 Drugs use in palliative sedation

Terminally ill patients experienced changes in drug absorption, metabolism and elimination processes. If deemed ethically possible, more comprehensive research would improve the knowledge with drug interaction and physiological alterations that take place in the final stages of life and enable the necessary dose adjustments to preserve the highest possible standard of care. The primary medications used in palliative care have had their pharmacokinetic features examined in recent studies, yielding helpful suggestions for clinical practice (Garetto et al. 2018: 955.)

According to the National Hospice and Palliative Care Organization, palliative sedation was a treatment that patients, families, and medical professionals should take into consideration to prevent intractable suffering of terminally ill patients, whereby, death was imminent (Diez- Manglano et al. 2020: 305). Terminally ill patients and their loved ones conveyed their wish for the patient to experienced peaceful death without suffering (Eun et al. 2017: 1013). According to Meesters et al. (2021), to relieved suffering at the end-of-life, reducing patient’s consciousness through the administration of sedative drugs was acceptable method (Meesters et al. 2021: 1). Therefore, the used of sedation was a therapeutic intervention to reduced the suffering and refractory symptoms as patients approached death (Schur et al. 2016: 1).

5.3.1 Sedative drugs

Frequently used drug in palliative sedation was benzodiazepine mainly midazolam (Diez- Manglano et al. 2020; Schur et al. 2016; Schildmann et al. 2022; Anquinet et al. 2013; Meesters et al. 2021; Vivat et al. 2019; Prado et al. 2018; Yokomichi et al. 2022;

Won et al. 2019; Caraceni et al. 2018 and Gamblin et al. 2020). Midazolam was used to treat other refractory symptoms such as dyspnea and delirium. It has many benefits compared to other benzodiazepines, such as a brief half-life and an immediate start of action, safe administration methods depending on the patient's condition. It was administred subcutaneously or intravenously, repeated bolus, continuous infusion, with a dose range from 5 to 120 milligrams per 24 hours, with evidenced of up to 1200 milligrams per 24 hours, and a wide dose range. Inter-individual variability was associated with metabolic variables, most likely through an inflammatory process, such as changes in the urine clearance of metabolites in hypoalbuminemia instances (Garetto et al. 2018: 955.)

If midazolam proved ineffective, other concomitant anti-psychotic neuroleptic drug particularly haloperidol was used after further consideration of causation (Diez-Manglano et al. 2020; Schur et al. 2016 and Caraceni et al. 2018). In many years, haloperidol has been used often in this context to treat delirium. Furthermore, it has been suggested as drug of choice and first-line treatment for delirium in a reputable practical reference to all aspects of palliative care. Better details were still needed on its titration time, hazards, ideal dose, and clinical efficacy. Haloperidol was metabolized through several processes that involved the enzymes uridine diphosphoglucose glucuronosyltransferase, carbonyl-reductase, and cytochrome P450 (CYP). This antipsychotic was usually initiated at a low dose from0.5–2.0 millligrams and progressively titrated until the intended effect is attained to prevent extrapyramidal and cardiovascular adverse effects. Haloperidol had metabolic changes related to hypoalbuminemia were linked to a relatively long terminal half-life, approximately 20 hours. Haloperidol and second-generation antipsychotics had been subject of some recent research that addressed the management of terminal delirium (Garetto et al. 2018: 957.)

5.3.2 Non sedative drugs

Pain and dyspnea were treated with opioids, if was prescribed to a patient undergoing palliative sedation for such symptoms, it was recommended that opioid must not be stopped. Nonetheless, morphine was not recommended for sedation like other main opioids since it was a non sedative in the traditional meaning of the word. Due to their simultaneous influence on particular symptoms, several medications were employed in

sedation procedures (Garetto et al. 2018: 957.) Researchers believed the use of opioids particularly morphine (Diez- Manglano et al. 2020 and Caraceni et al. 2018) was within the sedation regimen although not as a single drug.

6 Discussion of Findings

The purpose of this study was to described the used of palliative sedation in the end-of-life care as well as the drugs used in palliative sedation. Hence, this study aimed to provide further information and to gain more knowledge on the utilization of palliative sedation in end-of-life care that will guide nurses and other health care practitioners in their scope of practice. The collected and analysed data for this study reveals two main categories consisting of used of palliative sedation in end-of-life care and the drugs used in palliative sedation.

Results of this study showed that palliative sedation was considered appropriate in cases of refractory symptoms. According to Anquinet et al. (2013) and Van Deijck et al. (2016) symptom relief and not the hastening of death and to alleviate discomfort caused by refractory symptoms was the main indication of palliative sedation. Consistent with the articles, the most common reason to begin palliative sedation was delirium, either delirium itself or in conjunction with other symptoms. Apart from delirium, Caraceni et al. (2018) stated that dyspnea, pain and existential suffering were the next most common indications for the used of palliative sedation in end-of-life care. Subsequently, anxiety, agitation and fatigue were mentioned only in few articles without elaboration and further discussion. Though existential suffering was complicated since it pertains to a variety of symptoms, Schur et al. (2016) affirmed that it was uncertain to determine with conviction whether the symptoms were truly refractory since it did not always signify a severe stage of psychological decline. Accordingly, palliative sedation for existential suffering must be evaluated carefully.

As seen by the progressive reduction in symptom severity, palliative sedation was recognized to be effective. Professionals and the family of terminally ill patients both expressed a high degree of satisfaction, which they nearly universally deemed optimal. Sedative medication was primarily used for patients suffering from intractable symptoms at the end of life as claimed by Vivat et al. (2019). As to the treatment of refractory symptoms, the study of Mercadante et al. (2013) stated that benzodiazepines were the most common used drug in Palliative sedation particularly

midazolam. The midazolam doses were slightly increased 24 hours after initiating palliative sedation based on the clinical requirement and level of unconsciousness needed to control symptoms. Only one in three patients who lasted four days required an increase in dose, and the amounts were much lower than in earlier studies that were reported. Only a small percentage of patients who lasted longer than 24 hours required additional dose increments. Subsequently, Diez-Manglano et al. (2020) mentioned that midazolam was the most frequently used palliative drug and as the first-line agent according to Won et al. (2019). Whereas the study of Schur et al. (2016) added that midazolam is a short-acting benzodiazepine with muscle relaxant, anticonvulsant, and anxiolytic properties.

According to Prado et al. (2018), psychotropic neuroleptic drugs such as haloperidol were more suitable for the management of delirium and considered in combination with benzodiazepines. Aside from sedatives, the concomitant used of non sedative drugs such as opioids were considered. A significant number of the patients under sedation were on opioids, a class of medications frequently used to managed symptoms in the latter stages of life and primarily used to treat pain and dyspnea. As stated by Mercadante et al. (2013) opioids were maintained and administered through nonoral course having no intention to sedate. Additionally, Caraceni et al. (2018) claimed that morphine was an opioid administered in palliative sedation but never as a single drug.

Furthermore, Schur et al. (2016) added that other benzodiazepines such as lorazepam and diazepam were also given in palliative sedation as a concomitant drug, but no further discussion given supporting this claim. On the other hand, Yokomichi et al. (2022) also mentioned other neuroleptics like levomepromazine and chlorpromazine but no emphasis and elaboration on this claim.

7 Ethics and Validity

Research is the systematic study, reflection, experimentation, and observation with the purpose of advancing knowledge. Even though they may employ various methods to do so, all disciplines aimed to deepen our awareness of who we are and the world in which we live. Every study involving human subjects was primarily built on the participants' trust in scientists and researchers. Trust must be upheld through respecting the rights and human dignity of people who participated in the research. The demand for informed consent was a key ethical principle in research with human beings. Anybody

may have a brief or more serious loss in capacity. Ethical considerations must be considered while working with study subjects whose capacity was limited, for instance because of illness or age. Age, memory impairment or physical limits, for example, should not limit the freedom to choose whether or not to participate in research or the right to autonomy (TENK 2019: 11.)

Validity in qualitative research is defined by appropriateness of the tools, procedures, and data. The design, sampling, data analysis, and methodology all need to be valid, and the findings and conclusions must make sense given the sample and context (Leung 2015: 325.)

This study adhered to the ethical conduct of research throughout the entire process. The chosen publications used data from reputable primary sources and came from well-known databases. References from the Metropolia University of Applied Sciences libguides were used to expand our knowledge and become more familiar with the study topic and study questions. There was no requirement for translations because both the study questions and the articles used for the study were in English. Data analysis information was based on the actual study findings that were reported in the cited journals. This study was written with the intention of helping nurses and other health care practitioners, not of harming anyone. This study was created using descriptive literature review. No permission was required to perform the study, and no interviews or surveys of any kind were conducted. The study was written using the Metropolia University of Applied Sciences Guidelines for Written Assignments. The authors and researchers of the articles used as sources for this study were properly referenced (ARENE 2018: 6.) The study was submitted to the Turnitin application to have the amount of plagiarism checked in order to verify its validity. The school's information specialist assisted with the data base search, ensuring the accuracy of the key terms used throughout the study.

8 Strengths and limitations

This study presented clear and concise information as to the used of palliative sedation in end-of-life care, that is to treat refractory symptoms. The specific symptoms were identified as well as the drugs used in palliative sedation. Therefore, the purpose of the study was appropriately served by clearly answering the formulated research

questions. Articles included in the study were all academic which possess a quality assessment rating of 1 and 2 taken from reliable database sources.

The study process revealed lack of studies carried out on the subject matter which limits the acquisition of relevant knowledge as to the adequacy of information on efficacy of symptom relief and survival rate with the used of palliative sedation in end-of-life care. Our study focused on the use of palliative sedation in end-of-life care in general without mentioning a specific terminal illness. Prevalence of palliative sedation in different settings, as well as the role of nurses in palliative sedation were also limited in this study. Furthermore, studies carried out beyond the inclusion criteria as to the year of publication was another limitation of this study.

9 Conclusions and recommendations

The following conclusions were drawn based on the findings of this study:

- Palliative sedation is mainly use to treat refractory symptoms in end-of-life care.
- The most common refractory symptoms indicating the use of palliative sedation were delirium, dyspnea and pain which is consistent with the articles.
- The sedative drugs proven effective to use in the treatment of refractory symptoms is benzodiazepine particlularly midazolam which is consistent with the articles.
- Psychotropic neuroleptic drugs such as haloperidol is suitable for the management of delirium in combination with benzodiazepines.
- Other concomitant non sedative drugs used in end-of-life care is opioids mainly for the treatment of pain and dyspnea.

This study will introduce palliative sedation as treatment of refractory symptoms. It will increase the knowledge of nurses and further understand the use of palliative sedation and the drugs utilize to treat patients with terminal illness. The approach to patient treatment is multidisciplinary, thus it is in the best interest to be equipped with the necessary scientific knowledge and skills to carry out their task. It was observed that the attitude and nursing abilities had an impact on the management of patients with terminal illness. We had considered how we could help in raising the standard of patient care and safety after with this study. In addition, we also learned how crucial interprofessional cooperation is in providing quality care to patients, therefore, by presenting the used of

palliative sedation in end-of-life care, this study had the potential to increased the understanding and will help develop the skills of nurses and other health care practioners in providing end-of-life care.

Furthermore, the knowledge acquired during the entire process of the study was extremely valuable, emphasizing the value of critical thinking, ethical thought, and research work. It is essential for nurses to know where to find trustworthy, scientifically based information and identify academic research. We were able to assess the reliability and accuracy of the information.

Studies that will enhance the understanding of nurses and other health care practitioners in Palliative sedation in general is important as this study was limited on the use of palliative sedation to treat refractory symptoms and the drugs use in palliative sedation. The benefits of palliative sedation that recommend its utilization are not well discussed. There was few nursing research on the subject and focused mostly on medicine, therefore, the authors of the this study recommends further research as the study process revealed lack of studies on the subject matter. It is not a common practice but it has a great potential. More nursing study on the subject would be helpful because nurses are always the frontliner in providing healthcare and other services in healthcare, and it is critical that nurses understand how palliative sedation is used in various settings.

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Appendix 1. Summary of included articles

Author (s), Year, Country	Topic/ Title	Methodology/ Methods	Participants	Main Outcome	Limitations
1. Diez- Manglano et al. 2020 Spain and Argentina	Palliative Sedation in Patients Hospitalized in Internal Medicine Departments	Quantitative Cross-sectional, retrospective audit study	N= 1447 patients The study included 82 general hospital and 63 from other hospitals and 57 county. There were 10 patients who passed away in Internal medicine department in each hospital.	Palliative sedation for patients who dies in Internal medicine departments were given sedation more frequently than to those who were admitted to the hospital despite terminal illness condition.	The study was retrospective in nature and analysis came from medical records of patients. Ten patients deaths were reported in each hospital without considering the number of beds and admissions.
2. Eun, Hong, Bruera, Kang 2017 Korea	Qualitative Study on the Perceptions of Terminally Ill Cancer Patients and Their Family Members Regarding End-of-Life Experiences Focusing on Palliative Sedation	Qualitative In-depth interview	N=13 Participants included were terminally ill patient less than 3 months life expectancy.	Terminally ill cancer patients and their caregivers expressed ambivalent desires, simultaneously hoping to prolong life and to experience a peaceful death.	Trustworthiness of data, there was limited demographic nature of both caregivers and patients with terminal illness.
3. Shen et al. 2018 Tapei, Taiwan	Differential Family Experience of Palliative Sedation Therapy in Specialized Palliative or Critical Care Units	Quantitative Observational survey	N=143 Participants included were 81 from the PCU and 62 from the ICU.	The study's findings highlighted the need for health care providers to address family members' concerns about psychological testing and offer tools for identifying family members who may be more likely to experience grief. This helps to strengthen the current PST use guidelines, which place a strong emphasis on family-centered care.	The results' potential to be broadly applied was constrained by non-probability sampling and the limited sample size. The used of PST by HCPs was not investigated. Some information was not elicited, including the percentage of patients in the ICU on mechanical ventilation, the effectiveness of symptom alleviation, and the sufficiency of information obtained from HCPs.

4. Schur et al. 2016 Austria	Sedation at the end of life - a nation-wide study in palliative care units in Austria	Quantitative Retrospective chart interview	N= 2414 patients The study included patients who hied in Austrian palliative care between June 01, 2012 and May 2013 who were under sedation in the last two weeks of their life.	It confirmed that palliative sedation was a therapeutic intervention that was suitable and did not reduced the amount of time patients spend from the moment they were admitted to a palliative care unit or mobile care team until they died.	This study can't conclusively confirm or deny that sedation has a life-shortening effect because it only offers a general assessment of how palliative sedation affects actual survival. Another limitation was existential suffering was not given a clear operational definition.
5. Schildmann, Meesters, Bausewein 2022 Germany	Sedatives and Sedation at the End of Life in the Hospital	Quantitative Retrospective Cohort Study	N= 530 patients The median age was 77 years	This study shows that in the final week of their lives, most dying inpatients were given either modest dosages of sedatives that had a continuous impact or none at all. The data show variations in the way that sedatives were managed among departments as well as documented practice that deviates from guidelines.	Because some data were not systematically documented and could not be evaluated, the study's retrospective approach represents a significant limitation.
6. Anquinet et al. 2013 Belgium, Nether-lands, UK	Physicians' experiences and perspectives regarding the use of continuous sedation until death for cancer patients in the context of psychological and existential suffering at the end of life	Qualitative Interview	N= 39 Participants were cancer patients who had psychological and existential suffering (18 Belgium, 12 the Netherlands, and 9 UK), involving 35 physicians (13 Belgium, 11 the Netherlands, & 11 UK).	Patients were given continuous sedation mainly to those who suffered from physical symptoms, psychological symptoms and existential suffering.	A statistical generalization of the results was not possible due to the small num-ber of cases and interviews done for the study.

7. Meesters et al. 2021 Germany	“We don’t want to sedate him” - A qualitative interview study on intentions when administering sedative drugs at the end of life in nursing homes and hospitals	Qualitative Semi structured interview	N=49 13 Hospital Nurses, 12 Hospital Physicians, 12 Nursing home Nurses, 12 General practition-ers	All interviewed stressed that they wanted to alleviate the patient's suffering while yet allowing them to communicate as much as possible. Nursing home nurses in particular stressed that they make every effort to prevent any loss of consciousness, even if it means putting up with some degree of suffering.	Despite the attempts of purposive sampling, which included contact persons specifically being motivated to recruit less experienced healthcare professionals, the latter group was underrepresented, thus it's possible that their viewpoints weren't properly considered.
8. Mercadante et al. 2013 Italy	Palliative Sedation in Patients With Advanced Cancer Followed at Home: A Prospective Study	Quantitative Prospective study	N= 219 patients One hundred seventeen and 102 were surveyed during the study period in L’Aquila and Turin, respectively.	Intractable symptoms in the final stages of life can be effectively relieved with PS administered at home. It would be fascinating to assess any potential variations across acute palliative care units, hospices, and home care programs	Because it is difficult to guarantee that study groups were indeed comparable at baseline, statistical results may not always be trustworthy, particularly in the absence of a large sample size.
9. Vivat et al.2019 UK	Palliative care specialists in hospice and hospital/community teams predominantly use low doses of sedative medication at the end of life for patient comfort rather than sedation: Findings from focus groups and patient records for I-CAN-CARE	Qualitative Focus group review	N=27 Clinicians 10 physicians 17 senior nurses in London hospice or hospital/community palliative care .	All focus group members stated that they primarily utilized sedative medication to manage agitation or distress; they also stated that they chose medications and dosages based on each patient's unique needs; and they tried to use the lowest dosages necessary to make patients feel "comfortable," "calm," or "relaxed."	The generalizability of the study is constrained. Another limitation was that data from patient records was evaluated rather than by direct observation of patient care, therefore it was not possible to assume that the data accurately reflects the situations of the patients.

10. Prado et al. 2018 Brazil	Continuous palliative sedation for patients with advanced cancer at a tertiary care cancer center	Quantitative Retrospective Studies	N= 552 patients Patients that were admitted to hospital and died during hospitalization between March 01, 2012 and December 3, 2014.	Comparing the PS group to the non-sedated patient group, the study found no adverse effects on patient survival. For the sedated population, the survival time, which was expressed as the number of days from admission to death, was noticeably longer.	There was no consistent and routine procedure for grading symptoms before and during PS in the study. Patients' state of sedation or not was not a reliable indicator of survival.
11. Yokomichi et al. 2022 Japan	Effect of continuous deep sedation on survival in the last days of life of cancer patients: A multicenter prospective cohort study	Quantitative Prospective cohort study	N=1625 patients The median age was 74.	In patients with advanced cancer, continuous deep sedation with cautious dose adjustments was not linked to a lower chance of surviving in the latter stages of life.	The use of continuous deep sedation and its methodology were not entirely standardized. The outcomes were limited by unmeasured variables such as respiratory failure, psychological discomfort, and other sedative drugs.The results were limited due to the omitted population. Finally, patients who were not admitted to a PCU were not included in the generalization of the results.
12. Won et al.2019 South Korea	Clinical Patterns of Continuous and Intermittent Palliative Sedation in Patients with Terminal Cancer: A Descriptive, Observational Study	Qualitative Descriptive Observational Study	N= 306 patients Patients who received palliative sedation.	PS effectively manages refractory symptoms in cancer patients nearing the end of their lives without reducing their survival time.	Potential biases in interpersonal appraisal and retrospective analysis were the limitation of the study. Multicenter research is required in order to assess if the findings were generally applicable.

13. Caraceni et al. 2018 Italy	Palliative Sedation in Terminal Cancer Patients Admitted to Hospice or Home Care Programs: Does the Setting Matter? Results From a National Multicenter Observational Study	Quantitative Multicenter observational longitudinal study	N= 4276 Studies carried out in 38 HC and HS primary care services between January 2010 to December 2011.	Setting differences with indication to Palliative sedation prompted inquiries regarding the two contexts' comparability. The clinical experience showed that PS was more important procedure for dyspnea than for delirium. Consequently, it' was probable that some patients with delirium were better handled at home, whereas others with illnesses such as severe respiratory distress were more frequently admitted to HS. The overall increased frequency of sedative used in HS could be explained by a higher burden of challenging symptoms.	The lack of a standardized protocol for palliative sedation meant that the researchers treating patients also evaluated the results of the treatment, including the patients' awareness of their diagnosis and prognosis and the identification of refractory symptoms. This could have led to bias in the assessment of the effect.
14. Van Deijck et al. 2016 Netherlands	Level of Discomfort Decreases After the Administration of Continuous Palliative Sedation: A Prospective Multicenter Study in Hospices and Palliative Care Units	Quantitative Prospective observational multicenter study	N= 803 patients 76 years or older	This study showed that, although higher levels of discomfort were experienced in the final hours of life in certain sedated individuals, CPS was linked to a decreased in discomfort within a reasonable time frame.	The study's limitation was that it used a validated technique to track people with dementia who were cognitively impaired rather than patients who were sedated continuously.
15. Gamblin et al. 2020 France	Midazolam sedation in palliative medicine: retrospective study in a French center for cancer control	Quantitative Retrospective study	N=54 patients	Nearly 50% of instances involved refractory symptoms and acute consequences that pose an imminent risk to life, which were the most common reasons for using palliative sedation.	Due to the retroactive method of the study, there was a chance that the practices understudied may be underestimated due to insufficient traceability.

Appendix 2. Research journal quality assessment

Name of the Journal	Reference	Publisher	Score
Palliative Sedation in Patients Hospitalized in Internal Medicine Departments; Journal of Pain and Symptom Management	Diez-Manglano et al. 2020	Elsevier Inc.	2
Qualitative Study on the Perceptions of Terminally Ill Cancer Patients and Their Family Members Regarding End-of-Life Experiences Focusing on Palliative Sedation; Journal of Pain and Symptom Management	Eun et al. 2017	Elsevier Inc.	2
Differential Family Experience of Palliative Sedation Therapy in Specialized Palliative or Critical Care Units; Journal of Pain and Symptom Management	Shen et al. 2018	Elsevier Inc.	2
Sedation at the end of life - a nation-wide study in palliative care units in Austria; BMC Palliative Care	Schur et al. 2016	BMC Palliative Care	1
Sedatives and Sedation at the End of Life in the Hospital; Palliative Medicine	Schildmann, Meesters, Bausewein 2022	Deutsches Ärzteblatt International	1
Physicians' experiences and perspectives regarding the use of continuous sedation until death for cancer patients in the context of psychological and existential suffering at the end of life; Palliative Medicine	Anquinet et al. 2013	John Wiley & Sons, Ltd.	2
"We don't want to sedate him" - A qualitative interview study on intentions when administering sedative drugs at the end of life in nursing homes and hospitals; BMC Palliative Care	Meesters et al. 2021	BMC Palliative Care	1

Palliative Sedation in Patients With Advanced Cancer Followed at Home: A Prospective Study; Journal of Pain and Symptom Management	Mercadante et al. 2013	Elsevier Inc.	2
Palliative care specialists in hospice and hospital/community teams predominantly use low doses of sedative medication at the end of life for patient comfort rather than sedation: Findings from focus groups and patient records for I-CAN-CARE; Palliative Medicine	Vivat et al. 2019	Palliative Medicine	2
Continuous palliative sedation for patients with advanced cancer at a tertiary care cancer center; BMC Palliative Care	Prado et al. 2018	BMC Palliative Care	1
Effect of continuous deep sedation on survival in the last days of life of cancer patients: A multicenter prospective cohort study; Palliative Medicine	Yokomichi et al. 2022	Palliative Medicine	2
Clinical Patterns of Continuous and Intermittent Palliative Sedation in Patients with Terminal Cancer: A Descriptive, Observational Study; Journal of Pain and Symptom Management	Won et al. 2019	Elsevier Inc.	2
Palliative Sedation in Terminal Cancer Patients Admitted to Hospice or Home Care Programs: Does the Setting Matter? Results From a National Multicenter Observational Study; Journal of Pain and Symptom Management	Caraceni et al. 2018	Elsevier Inc.	2
Level of Discomfort Decreases After the Administration of Continuous Palliative Sedation: A Prospective Multicenter Study in Hospices and Palliative Care Units; Journal of Pain and Symptom Management	Van Deijck et al. 2016	Elsevier Inc.	2
Midazolam sedation in palliative medicine: retrospective study in a French center for cancer control; BMC Palliative Care	Gamblin et al. 2020	BMC Palliative Care	1